ANTIBIOTIC-RESISTANT BACTERIA COLONISATION PATTERNS IN DIFFERENT NEONATAL POPULATIONS ACROSS EUROPEAN NEONATAL INTENSIVE CARE UNITS

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Background:

- Colonisation pressure is a major contributor to the spread of resistant bacteria in neonatal units
- **Pre-trial colonisation feasibility study** to characterize baseline colonization pressure at neonatal-unit level
- Feasibility study to inform **NeoDeco study*** (*Optimising kangaroo care to reduce neonatal severe infection/sepsis and resistant bacterial colonisation among high-risk infants in neonatal intensive care: a pragmatic, multicentre, parallel cluster randomised hybrid implementation-effectiveness study)

> Gaps in knowledge with Kangaroo Care:
- Unknown effects of immediate and prolonged skin-to-skin contact on bacterial resistance colonisation pressure
- Unknown if skin-to-skin contact has the same beneficial effects on sepsis and mortality of high-risk infants in HIC as it has in LMICs

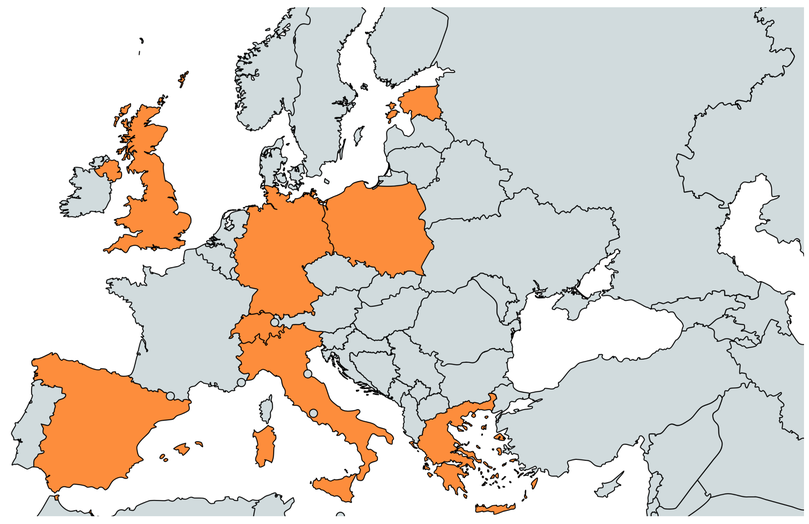
NICU admissions accounts for 5-8% of all live births in HICs and around 1 million within European region yearly[1]

Globally, 10.6% live births estimated to occur prematurely[1]
- Risk of severe bacterial infections due to immunological immaturity, longer hospital stay, indwelling devices, invasive procedures, etc.
- High/repeated antibiotic exposure during admission may contribute to emergence of resistant bacteria[2,3]

Challenges in preventing resistance bacterial colonisation in NICUs[4]
- Open bay or multiple cot rooms
- Staff managing multiple patient with lots of equipment / understaffing

Methods:

- **Feasibility study: 4 cross-sectional surveys (point-prevalence surveys, PPS)** in 1-month – variable intervals of 4, 7 and 14 days
- **23 sites** (**8** European countries)
- **Skin swabs** and **faecal samples** collected from **all infants** present on unit on day of survey
- Data collected on REDCap
- Infants present on multiple surveys contributed longitudinal data
- Infants born **<32 weeks**' gestational age defined as "**high-risk**"
- **DNA extraction** (NucliSENS easyMAG, bioMérieux)
- **RT-qPCR** detection of
  - **carbapenemases** in stool (CBPs; Carbaplex-IVD PCR, Bruker);
  - **extended-spectrum-beta-lactamases** in stool (ESBLs; Ba04646149_s1, Ba04646127_s1, ThermoFisher);
  - **vancomycin-resistant enterococci** in stool (VREs; VRE, Geneproof);
  - **Methicillin-resistant *Staphylococcus aureus* (MRSA)** in skin swabs (MRSA; Diarella MRSA-SeqC, Gerbion).



Gene targets of interest in stool samples

Carbapenem resistance: *bla*$_{KPC}$, *bla*$_{NDM}$, *bla*$_{VIM}$, *bla*$_{IMP}$, *bla*$_{OXA-48}$

Extended-spectrum beta-lactamase: *bla*$_{CTX-M}$ group1, *bla*$_{CTX-M}$ group9

Vancomycin resistance: *vanA, vanB*

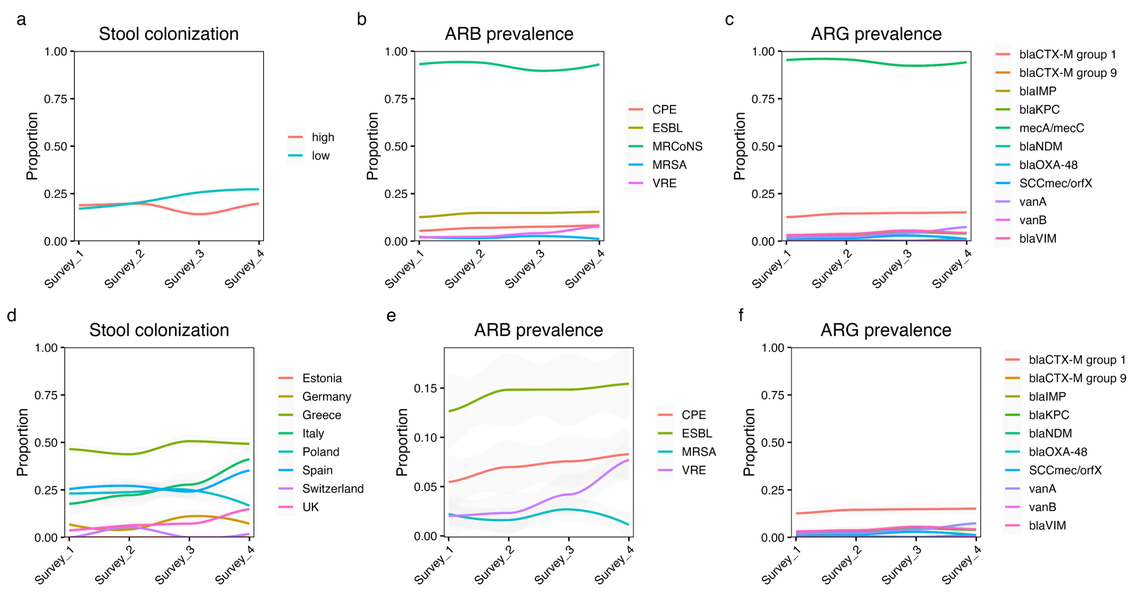
Antibiotic resistant bacterial (ARB) colonisation was defined as the detection of at least one target gene in an infant's stool

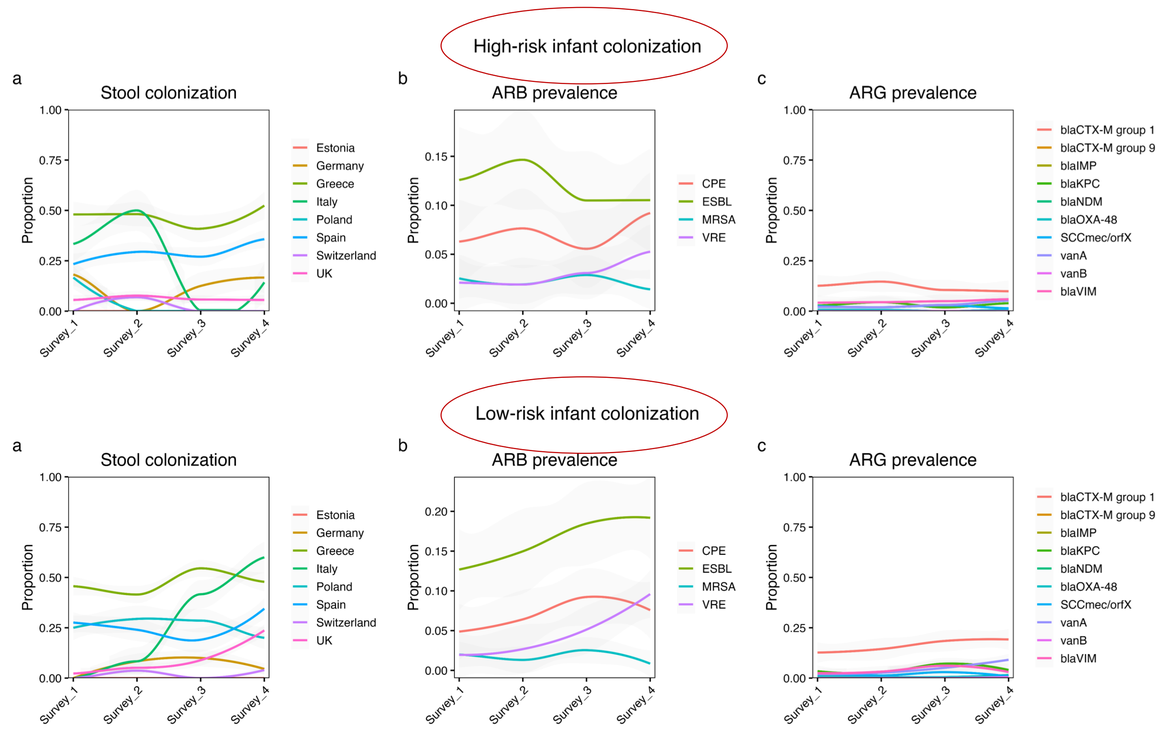
Results:

- **20.5% (288/1399) stool samples** positive for ARBs
- 36/92 surveys did not identify any ARB colonisation (varied by country)
- Overall, **ESBLs** (14.4%, *bla*$_{CTX-M}$ group1) were most prevalent, followed by **CBPs** (7.1%; mainly *bla*$_{KPC}$ and *bla*$_{VIM}$), and **VREs** (4.1%, *vanA*).
- 38.5% of colonized samples were from **high-risk** infants (111/614, **18.1%**), compared to 61.5% from **low-risk** infants (177/785, **22.5%**) (**p=0.04**)
- Resistant colonization differed significantly by country and site (**p<0.001, range 0.0%-94% for individual sites**)
- Gut colonization rate stability over time was ARB/ARG-dependent
- CBP and ESBL positivity remained stable over time (p>0.05); only **VRE colonization increased significantly** from 2%-7.7% during the study period (**p= 0.001**); MRSA skin colonization was rare (2.7%)

By risk group:

- CBP and ESBL positivity remained stable over time
- **significant difference** in the proportion of **ESBL-colonised** samples (low>high-risk, 16.3% vs. 12.1%)
- **VRE colonisation increased significantly for low-risk infants** from 2%-9.6% (p= 0.001)





Conclusions:

> Antibiotic-resistant bacteria/gene (ARB/ARG) colonization prevalence varied considerably across Countries and neonatal units, being highest in southern Europe.

> Stability of colonization rate/PPS varied for different ARBs/ARGs.

> ARB colonization prevalence not associated with proportion of high-risk infants on the unit

> The proportion of colonized low-risk infants was significantly higher.

Learn more about the NeoIPC Project here!

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